REMARKS

Claims 102-151, 152-156 and 158-160 are pending in this application. Claims 117-150, 152-156 and 158-160 have been withdrawn. Claims 104 and 107 are amended herein to correct informalities, as suggested by the Examiner. Claim 116 is amended as suggested by the Examiner. The specification, including the Abstract, has been amended to correct various informalities noted by the Examiner and as clarified herein. The amendments are fully supported by the specification as originally filed. Claims 102-116 and 151, as amended herein, are currently under consideration by the Examiner.

SEQUENCE COMPLIANCE

In response to the notice to comply with the requirements for patent applications containing nucleotide and/or amino acid sequence disclosures, applicants provide herewith an sequence listing including the two sequences noted by the Examiner as appearing in Figure 12 but not contained in the sequence listing previously submitted. Applicants have also amended the legend of Figure 12 to indicate provide sequence identifiers for each sequence appearing in figure 12 and corrected paragraph 0258 to delete reference to Seq ID No. 80. The amendments are supported by Figure 12 as originally filed.

OBJECTIONS TO THE SPECIFICATION

On pages 4-5 of the Office Action the Examiner objects to the specification for various informalities and typographic errors.

A revised Abstract is submitted herein as requested by the Examiner. The new abstract is fully supported throughout the specification as originally filed.

As discussed above in under the heading "Sequence Compliance", the objections to the sequence appearing in Figure 12 and in Example 8 have been obviated by amendment to the specification and by submission of a revised sequence listing.

The Examiner objects to the statement regarding incorporation by reference. However, this statement is explicitly permitted by 37 CFR §1.57(d) and, accordingly, withdrawal of the objection is requested..

Claims 104 and 107 have been amended to correct the typographic errors, noted by the Examiner.

In view of the foregoing, applicants respectfully request withdrawal of the objections to the specification.

INDEFINITENESS REJECTION

Independent claim 102, and corresponding dependent claims 103-115 are rejected under 35 USC §112, second paragraph, as indefinite. Specifically, the Examiner asserts that it is unclear whether ⌜ and ⌝ as shown in claim 102 represent methylene groups or cyclization of Formula (IV). Applicants respectfully traverse the rejection.

The skilled artisan would understand that the linking features ⌜ and ⌝ are a conventional manner of inidicating cyclization of the structure as shown, and the 90° angle shown in the link is present merely because of the constraints of typography. This is demonstrated by consideration of, for example, Scheme 3 in the specification, where cyclization of the side chains of lysine and aspartic acid are shown. The skilled artisan will recognize that this cyclization occurs via amide bond formation between the lysine ε-amino group and the aspartic acid β-carboxylic acid function and that the linkage ⌐¬ as shown merely serves to indicate this cyclization, rather than indicating the presence of an ethylene linkage. Accordingly, it would be entirely inconsistent with the specification to construe the linking features as indicating methylene groups. Nevertheless, to further clarify the nature of the linkages in claim 102, applicants have amended the claim to replace ⌜ and ⌝ with arcs. Accordingly, applicants respectfully submit that claim 102 and corresponding dependent claims fully comply with §112, second paragraph, and request withdrawal of the rejection.

Claims 102-115 also are rejected as indefinite. Specifically, the Examiner asserts that it is unclear what is meant by "residues" in the context of a peptide, and “a group that mimics an amino acid side chain.” Applicants respectfully traverse.

With respect to the term “residue” within a peptide, this is a standard term that indicates a single amino acid within that peptide. Thus, a peptide of 5 residues is one that contains 5 amino acids. The *IUPAC Compendium of Chemical Terminology,* 2nd Edition (1997) (available at *www.iupac.org/goldbook/A00279.pdf*, retrieved December 29, 2010) provides the following definition:

> **amino-acid residue (in a polypeptide)**
> When two or more amino acids combine to form a *peptide*, the elements of water are removed, and what remains of each amino acid is called an amino-acid residue. α-Amino-acid residues are therefore structures that lack a hydrogen atom of the amino group (–NH–CHR–COOH), or the hydroxyl moiety of the carboxyl group (NH2–CHR–CO–), or both (–NH– CHR–CO–); all units of a peptide chain are therefore amino-acid residues.

Accordingly, applicants respectfully submit that the term "residue" in the context of the present application has a meaning that is clear and well understood in the art. Withdrawal of the rejection respectfully is requested.

With respect to the term "a group that mimics an amino acid side chain," applicants point out that this term clearly is defined at paragraph 67 of the specification thus:

> Suitable groups that mimic an amino acid side chain are any natural or unnatural amino acid side chain that is attached to the N-terminal amino group of the peptide through a carbonyl group derived from a carboxylic acid by formation of an amide bond. Suitable mimics of amino acid side chains include, but are not limited to: $CH_3CH_2C(O)(CH_2)_uC(O)$-, $NH_2(NH=)CNHC(O)(CH_2)_uC(O)$-, $H_2NC(O)(CH_2)_2C(O)(CH_2)_uC(O)$-, $HOC(O)(CH_2)_2C(O)(CH_2)_uC(O)$-, $HS(CH_2)_2C(O)(CH_2)_uC(O)$-, $H_2NC(O)(CH_2)_3C(O)(CH_2)_uC(O)$-, $HOC(O)(CH_2)_2C(O)(CH_2)_uC(O)$-, (4- imidazolyl)$(CH_2)C(O)(CH_2)_uC(O)$-, $CH_3CH_2CH(CH_3)CH_2C(O)(CH_2)_uC(O)$-, $(CH_3)_2CH(CH_2)_2C(O)(CH_2)_uC(O)$-, $H_2N(CH_2)_5C(O)(CH_2)_uC(O)$-, $CH_3S(CH_2)_3C(O)(CH_2)_uC(O)$-, $Ph(CH_2)_2C(O)(CH_2)_uC(O)$-, $Ph(CH_2)_4C(O)(CH_2)_uC(O)$-$_3$ $HO(CH_2)_2C(O)(CH_2)_uC(O)$-, $HOCH(CH_3)CH_2C(O)(CH_2)_uC(O)$-, (3-indolyl)$(CH_2)_2(CH_2)_uC(O)$-, (4-hydroxyphenyl)$(CH_2)_2C(0)(CH_2)_uC(0)$-, (4-hydroxyphenyl)$(CH_2)_3C(O)(CH_2)_uC(O)$-, . $(CHa)_2CHCH_2C(O)(CH_2)_uC(O)$-, $CH_3CH_2CH_2C(O)(CH_2)_uC(O)$-, $C_6H10CH_2C(O)(CH_2)_uC(O)$-, $C_5H_8CH_2C(O)(CH_2)_uC(O)$-, $CH_3C(O)(CH_2)_uC(O)$-, $CH_3(CH_2)_4C(0)(CH_2)_uC(O)$-, $CH_3(CH_2)_5C(O)(CH_2)_uC(O)$-, $HOC(O)CH_2C(O)(CH_2)_uC(OK$ $HS(CH_2)C(O)(CH_2)_uC(O)$-, $H_2N(CH_2)_4C(O)(CH_2)_uC(O)$- and $HOCH_2C(O)(CH_2)_uC(O)$-, wherein u is 0 or an integer from 1 to 10.

Accordingly, the specification not only provides a clear definition of a group that mimics an amino acid side chain but also provides a large number of suitable examples of such groups. Applicants respectfully submit that one skilled in the art is fully apprised of the nature and identity of "a group that mimics an amino acid side chain"{ and request withdrawal of the rejection.

WRITTEN DESCRIPTION

Claims 102-115 and 151 are rejected under 35 U.S.C. §112, first paragraph, for lack of written description. Specifically, the Examiner asserts that the claims do not describe a single structural feature nor does the specification clearly define or provide examples of what qualifies as compounds of the claimed invention. The Examiner further alleges that the claims lack written description for failure to disclose a correlation between function and structure of the compounds beyond the compounds disclosed in the Examples. Applicants respectfully traverse.

The MPEP states:

> "The courts have described the essential question to be addressed in a description requirement issue in a variety of ways. An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). Under *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed. The test for sufficiency of support in a parent application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter." *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985) (quoting *In re Kaslow*, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983)).

See MPEP §2163.02, Rev. 6, September 2007 at 2100-186.

What is known in the field and accessible to all need not be repeated in the specification. *Falkner v. Inglis,* 448 F.3d 1357, 1365-68, (Fed. Cir. 2006). In *Falkner* the court made clear that mere the absence of examples involving poxviruses in the Inglis applications did not render the written description inadequate. As explained in *LizardTech, Inc. v. Earth Resource Mapping, PTY, Inc.*:

> "A claim will not be invalidated on section 112 grounds simply because the embodiments of the specification do not contain examples explicitly covering the full scope of the claim language. That is because the patent specification is written for a person of skill in the art, and such a person comes to the patent with the knowledge of what has come before. Placed in that context, it is unnecessary to spell out every detail of the invention in the specification; only enough must be included to convince a person of skill in the art that the inventor possessed the invention and to enable such a person to make and use the invention without undue experimentation."

See LizardTech, Inc. v. Earth Resource Mapping, PTY, Inc. 424 F.3d 1336, 1345

(Fed.Cir.2005) (citing *Union Oil Co. v. Atl. Richfield Co.,* 208 F.3d 989, 997 (Fed.Cir.2000); *In re GPAC Inc.,* 57 F.3d 1573, 1579 (Fed.Cir.1995)).

In this context, Applicants refer the Examiner, as discussed above, that:

> Whenever the issue arises, the fundamental factual inquiry is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. See, e.g., *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. See, e.g., *Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997); *Amgen, Inc. v. Chugai Pharmaceutical*, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991) (one must define a compound by "whatever characteristics sufficiently distinguish it").
>
> The subject matter of the claim need not be described literally (i.e., using the same terms or *in haec verba*) in order for the disclosure to satisfy the description requirement….

See MPEP §2163.02, Rev. 6, September 2007 at 2100-186.

In the instant case, the claimed compounds are clearly defined by a chemical formula of the type that is present in tens of thousands of, for example, pharmaceutical patent applications filed each year. One skilled in the art readily can appreciate the nature of the claimed compounds and, based upon the clear description provided in the specification, can understand the nature of the three dimensional structure imposed upon the compounds by the given formula. It is not clear to applicants why more is needed.

This is not a case such as *Gosteli*, cited by the Examiner, where the description of two compounds was found to be insufficient to describe a later-defined genus where that genus was not defined in the original specification. Rather, the instant specification clearly set forth the generic structure cited in the claim 102. Nor is this case like *Regents of the University of California v. Eli Lilly* where the disclosure of a single rat insulin gene was held insufficient to provide a written description of all mammalian insulin genes. In the *Regents* case no attempt was even made to define what other mammalian insulin genes would look like – rather, their structure was defined only in terms of the fact that they encoded insulin. The instant case

could not be more different – an explicit structural formula is provided, showing points of attachment, Markush groups of permissible substituents, and the positioning of the cyclizing linkage that produces the characteristic helical structure of the claimed compounds. The permissibly substituents are clearly defined in the specification in a manner that would be recognized by a person skilled in the art and the Examiner has failed to provide any concrete reasoning as to why these descriptions and definitions are insufficient under §112, first paragraph. The reasoning provided by the Examiner would invalidate almost all pharmaceutical patents which contain the same types of generic formulae set forth in instant claim 102. Applicants respectfully submit that the Examiner has failed to meet the applicable burden of demonstrating the claims lack an adequate written description and request withdrawal of the rejection.

The instant application describes cyclic pentapeptide modules that are highly alpha-helical in their own right in water even when subjected to denaturing conditions and further describes how these modules, either singly or as oligomers, can be used as 'scaffolds' that mimic alpha helices in larger peptides or polypeptides. These cyclic and multi-cyclic structures permit variations at 3 of the 5 component amino acids of each cyclic pentapeptide module (shown as Xaa in claim 102) without loss of the helical structure and thus are suitable for general mimicry of short alpha-helical protein segments that, for example, bind receptors/ligands, and confer major advantages of conformational and proteolytic stability over linear peptides.

Moreover, contrary to the Examiner's assertions, the instant specification is replete with guidance in how the claimed pentapeptide modules may be designed and synthesized (*see*, for example, paragraph [0113]-[0121]). The specification also describes how to mimic multiple turns of an alpha-helical binding array by linking consecutive pentapeptide modules (*see*, for example, paragraph [0123]-[0126], [0202]-[0210]). Finally, the specification also exemplifies several peptides falling within the scope of Formula IV as defined in the pending claims including SEQ ID NOs: 46 (Example 5), 47 (Example 6), 57-64 (Example 9) and 76-70 (Example 15). Significantly, all of these peptides adopt an alpha-helical structure consistent with the teachings in the specification.

Further examples of peptides falling within the scope of the instant claims have been described by the inventors in subsequent publications in prestigious scientific journals. See, for example Harrison *et al.* (*Proc. Natl. Acad. Sci. U.S.A.,* 107:11686-11691 (2010) , appended hereto), which discloses two bicyclic alpha-helix mimetics, a RSV mimetic: (structure 20) and a CSP-1 mimetic (structure 22) with structural and *in vitro* data. In

particular, this publication further proves that back-to-back cyclic pentapeptide modules are highly alpha-helical by CD (61%) and NMR spectroscopy. The RSV mimetic was shown to be a potent inhibitor of RSV fusion (*see*, for example, page 11688, second column, second paragraph) and the CSP-1 mimetic was shown to have potent antibacterial activity (*see*, for example, page 11688, second column, fourth paragraph). In another publication (Harrison *et al.*, *J. Med. Chem.*, *In Press*, appended hereto) the inventors describe how (6,10; 7,11) bicyclo-FGGFT-[KARD]-[KARKLD]-NH_2, another compound that falls within the generic formula of claim 102, functions as a nociceptin analogue and an agonist of ERK phosphorylation in neuroblastoma cells.

In sum, the present specification explicitly sets forth a structural formula that clearly defines the claimed compounds, explicitly states which amino acids can be varied and how the cyclic compounds are linked. The structure also defines how multiple modules the means of constraining them, as well as how to link these modules side by side to produce peptides that mimic alpha helices in larger peptides. It is respectfully submitted, therefore, that the claims are fully compliant with the strictures of §112, first paragraph, and withdrawal of the rejection respectfully is requested.

CLAIM OBJECTION AND ALLOWABLE SUBJECT MATTER

The Examiner objects to claim 116 as being dependent upon a rejected base claim, but state that the claim would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Claim 116 has been amended as suggested and allowance of this claim therefore is solicited.

CONCLUSION

It is respectfully submitted that the application is in condition for allowance, and a notice of allowance is solicited at the earliest possible time. In the event the Examiner requires any further information, or would like to schedule an interview to advance prosecution in this application, the Examiner is encouraged to contact Applicants' undersigned representatives.

Respectfully submitted,

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